Joint Trust Guideline for the Antibiotic Treatment of Infective Endocarditis (IE) in Adults

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Joint Trust Guideline for the Anitbiotic Treatment of Infective Endocarditis (IE) in Adults

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Previous Title/Amalgamated Titles	Date Revised
None	Not applicable

Distribution Control

Printed copies of this document should be considered out of date. The most up to date version is available from the Trust Intranet.

Consultation

The following were consulted during the development of this document:
Cardiology Consultants
Antimicrobial Subcommittee
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Monitoring and Review of Procedural Document

The document owner is responsible for monitoring and reviewing the effectiveness of this Procedural Document. This review is continuous however as a minimum will be achieved at the point this procedural document requires a review e.g. changes in legislation, findings from incidents or document expiry.

Relationship of this document to other procedural documents

This document is a clinical guideline applicable to Norfolk and Norwich University Hospitals and James Paget University Hospitals.

Joint Trust Guideline for the Anitbiotic Treatment of Infective Endocarditis (IE) in Adults

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Joint Trust Guideline for the Anitbiotic Treatment of Infective Endocarditis (IE) in Adults

1.

1.1. Rationale

This guideline was written to ensure appropriate treatment for adult patients with endocarditis. The recommendations were taken from the guidelines on the antibiotic treatment of endocarditis in adults from the British Society of Antimicrobial Chemotherapy (BSAC) published in 2004 and updated BSAC guidelines published in 2012. Randomized controlled trials are lacking and therefore the BSAC paper was written on a consensus approach.

1.2. Objective

The objective of the Joint Guideline for the Antibiotic Treatment of Infective Endocarditis (IE) in Adults is to ensure appropriate prescribing and monitoring of antibiotics used in the treatment of bacterial endocarditis.

1.3. Scope

The scope of this guideline is to cover proven or suspected infective endocarditis. The guideline includes native valve endocarditis (NVE) and prosthetic valve endocarditis (PVE). PVE includes prosthetic valves of all types, annuloplasty rings, intracardiac patches and shunts. It does not include IE related to pacemakers, defibrillators or ventricular assist devices.

1.4. Glossary

The following terms and abbreviations have been used within this document:

Term	Definition
NVE	Native valve endocarditis
PVE	Prosthetic valve endocarditis

2. Responsibilities

Medical staff – will prescribe antibiotics in endocarditis in accordance with this policy.
Nursing staff – will administer antibiotics in accordance with this policy.
Pharmacy staff – will check prescriptions in accordance with this policy.

3. Policy Principles

3.1. Broad recommendations

From the start, for all patients with suspected or confirmed endocarditis:

a. **Consult with microbiology.**
b. **Involve a cardiologist regardless of the age of the patient.**
c. **ECHO requests are largely declined if the patient has had previously poor echo windows or previously recently known normal native valves on echo. Priority is given to Staph aureus bacteraemia, previous endocarditic patients, those with valve prostheses, high clinical suspicion i.e. raised CRP, murmur, positive urine dipstick, radiological evidence of emboli. A normal echo doesn't exclude endocarditis.**
d. **The cardiologist should consider whether consultation with a cardiac surgeon is required, particularly with prosthesis. Over 50% of patients require surgery as part of their treatment – see page 6 for further details.**

4. Microbiological Diagnosis

4.1. Blood cultures

Blood cultures remain a cornerstone of the diagnosis of IE cases and should be taken prior to starting treatment in all cases. Meticulous aseptic technique is required to reduce the risk of contamination with skin commensals which can lead to misdiagnosis.

There is no evidence to support the commonly perpetuated view that blood cultures should be taken from different sites. **Taking blood cultures at different times is critical** to identifying a constant bacteraemia, a hallmark of endocarditis. Bacteraemia is continuous in IE rather than intermittent so positive results from only one set out of several should be viewed with caution.

4.2. When and How to Take

- In patients with a *chronic or subacute presentation*: Take 3 sets of optimally filled blood cultures from peripheral sites with ≥ 6 h between them prior to commencing antibiotic therapy.
- In patients with suspected IE and *severe sepsis or septic shock* at time of presentation: Take 2 sets of optimally filled blood cultures at different times within 1 hour (or less depending on clinical situation) prior to commencing antibiotic therapy (to avoid undue delay in starting empirical antibiotics)
- In patients who have suspected IE but are already on antibiotic therapy, consider stopping treatment and performing 3 sets of blood cultures off antibiotics. Antibiotic therapy may need to be stopped for 7-10 days before blood cultures become positive.
- Repeat blood cultures if a patient is still febrile after 7 days of treatment.

- Once a microbiological diagnosis has been made, routine repeat blood cultures are not recommended.
- Avoid sampling of intravascular lines, unless part of paired through-line and peripheral sampling to diagnose concurrent intravascular catheter-related bloodstream infection.
- Avoid sampling from a groin sinus to take a blood culture in groin-injecting intravenous drug users.
- All patients with *Staphylococcus aureus* bacteraemia or candidaemia require echocardiography (ideally within first week of treatment or within 24 hours if there is other evidence to suggest infective endocarditis).

4.3. Serology

- In patients with blood culture negative IE, serological testing for Coxiella should be performed. Bartonella serology is currently not available.
- In patients with blood culture negative IE, routine serological testing for Chlamydia, Legionella and Mycoplasma should only be considered if the results of the above are negative.
- Consider Brucella in patients with negative blood cultures and a risk of exposure (dietary, occupational or travel).
- Candida antibody and antigen tests should not be used to diagnose Candida IE.

5. Antibiotic Treatment

In general, intravenous therapy is recommended to ensure adequate dosing and administration for an infection with high mortality. Recommended antibiotics include penicillins (such as penicillin, amoxicillin and flucloxacillin), gentamicin, glycopeptides (such as vancomycin and teicoplanin) and B-lactams such as meropenem or ceftriaxone.

5.1. Home Therapy

Home/ community/ outpatient therapy has been described. Suitability for home therapy will depend on the patient, infrastructure support and susceptibility of the infecting organism.

This should only be considered for stable patients, and only undertaken after discussion between consultant cardiologist and consultant microbiologist. Patients being managed this way need to be carefully monitored for side effects as well as their response to therapy.

5.2. Oral treatment

In stable patients agents with oral bioavailability that are close to that achieved with IV administration can be given orally provided the patient can tolerate oral medicine and is absorbing from the GI tract. Ciprofloxacin, linezolid and rifampicin have excellent oral bioavailability. Occasionally, particularly in IV drug users, problems obtaining or maintaining safe IV access means that oral therapy may be the safest treatment option. Consult microbiology for advice.

5.3. Empirical Treatment Regimens

Empirical therapy should be directed towards the most common causes of endocarditis. Empiricial regimens for patients with suspected endocarditis should be based on severity of infection, type of valve affected and risk factors for unusual or resistant pathogens.

If the patient is septic, haemodynamically compromised and endocarditis is strongly suspected; take 2 sets of blood cultures and start empirical antibiotics as suggested. (The imperative to treat septic shock takes precedence over the need to make an accurate diagnosis in this setting).

If the patient with suspected IE is clinically stable wait for the results of blood cultures before starting any antibiotics.

If the diagnosis of IE is in doubt, the patient is clinically stable and has already received antibiotics consider stopping the antibiotics and reculture.

In severe renal impairment, penicillin allergy, if an alternative is not specified, or if an unusual organism is cultured, always consult microbiology.

5.4. Penicillin Allergy

Patients with a history of anaphylaxis, laryngeal oedema, bronchospasm, hypotension, local swelling, urticaria or pruritic rash, occurring immediately after a dose of penicillin are at potential increased risk of immediate hypersensitivity to beta-lactams and should not receive prophylaxis with a beta-lactam antibiotic, e.g. cefuroxime. Patients with a history of penicillin allergy should be reviewed to exclude a non- immunological adverse reaction, e.g. diarrhoea, vomiting, non-specific maculopapular rash or an experience wrongly attributed to the antibiotic, e.g. ampicillin and Epstein-Barr virus infection

5.5. Culture Negative Endocarditits

When the diagnosis is strongly suspected clinically but repeated optimally taken cultures reveal no bacterial growth the decision as to whether to continue with empirical antibiotics or change to other antimicrobials should be taken jointly by the cardiologist and microbiologist involved.

5.6. Indications for Cardiac Surgery

A surgical opinion should be sought at the earliest opportunity for

- Every patient with endocarditis affecting intracardiac prosthetic material.
- Every patient with endocarditis and any of the indications in the table below.

The timing of surgery should be judged on a case-by-case basis but the relative urgency of different indications is given in the below table. Samples of valve or other infected tissue should be sent for microbiological and histopathological investigation.

5.7. Heart Failure
Aortic or mitral IE with:

1. Severe acute regurgitation or valve obstruction causing refractory pulmonary oedema / shock (emergency).
2. Fistula into a cardiac chamber or pericardium causing refractory pulmonary oedema / shock (emergency).
3. Severe acute regurgitation or valve obstruction and persisting heart failure or echocardiographic signs of poor haemodynamic tolerance (urgent).
4. Severe regurgitation and no heart failure (elective).

5.8. Uncontrolled infection

1. Locally uncontrolled infection including abscess, false aneurysm, enlarging vegetation (urgent).
2. Persisting fever and positive blood culture for ≥ 10 days after commencing appropriate antimicrobial therapy (urgent).
3. Infection caused by fungi or multi resistant micro organisms (urgent / elective).

5.9. Prevention of embolism

1. Aortic or mitral IE with large vegetations (>10mm) resulting in one or more embolic episodes despite appropriate antibiotic therapy (urgent).
2. Aortic or mitral IE with large vegetations (>10mm) and other predictors of complicated course like heart failure, persistent infection or abscess (urgent).
3. Isolated very large vegetations >15mm (urgent)

6. Treatment Tables

- Treatment recommendations for **Empirical therapy**
- Treatment recommendations for **Staphylococcus Endocarditis**
- Treatment recommendations for **Streptococcal Endocarditis**
- Treatment recommendations for **Enterococcal Endocarditis**
- Treatment recommendations for **Miscellaneous types of endocarditis**
- Treatment recommendations for **Gram negative Endocarditis**
- Treatment recommendations for **Fungal Endocarditis**
- Summary table for **dosage and monitoring of antimicrobials**

6.1. Treatment recommendations for Empirical Therapy

***Table 1*: Recommendations for Empirical Therapy (until the organism and sensitivity is available)**

1. NVE Indolent presentation		
Amoxicillin + **(optional)** Gentamicin*	2g IV 4 hourly 1mg/kg IV 12 hourly	If patient is stable, ideally await blood cultures. Better activity against enterococci and many HACEK microorganisms compared with benzylpenicillin **Use Regimen 2 if genuine penicillin allergy** The role of gentamicin is controversial before culture results are available
2. NVE, severe sepsis (no risk factors for Enterobacteriaceae*, Pseudomonas*)		
Vancomcyin# + Gentamicin*	As per policy 1mg/kg IV 12 hourly	Vancomycin - Pre dose levels 15-20mg/L In severe sepsis, staphylococci (including methicillin-resistant staphylococci) need to be covered. If allergic to vancomycin, replace with daptomycin (Consultant Microbiologist approval required) If there are concerns about nephrotoxicity /acute kidney injury use ciprofloxacin in place of gentamicin.
3. NVE, severe sepsis (AND risk factors∞ for Enterobacteriaceae*, Pseudomonas*)		
Vancomycin**#** + Meropenem	As per policy 2g IV 8 hourly	Vancomycin - Pre dose levels 15-20mg/L Will provide cover against staphylococci (including methicillin-resistant staphylococci), streptococci, enterococci, HACEK, Enterobacteriaceae and P. *aeruginosa*
4. PVE pending blood cultures or with negative blood cultures		
Vancomycin**#** + Rifampicin + Gentamicin*	As per policy 300mg – 600mg PO/IV 12 hourly 1mg/kg IV 12 hourly	Vancomycin - Pre dose levels 15-20mg/L Always use oral rifampicin if oral route available. Use 300mg BD dose of rifampicin if CrCl< 30mL/min

Notes:
NVE, native valve endocarditis; PVE, prosthetic valve endocarditis
Monitoring required. Caution in renal impairment – may need to reduce the dose- see page 13
*****Dose according to ideal body weight – see page 13. Monitoring required –see notes on page 13. Caution in renal impairment. May cause nephrotoxicity

∞ risk factors include colonisation with MRSA or extended-spectrum B-lactamases (ESBL) producing Enterobacteriaceae, or IV drug use.

6.2. Treatment Recommendations for Staphylococcus Endocarditis

Table 2: Summary of treatment recommendations for staphylococcus endocarditis

NVE, methicillin-susceptible *Staphylococcus* spp.			
Flucloxacillin	2g IV 6 hourly (<85Kg) 2g IV 4 hourly (>85kg)	4 weeks	
NVE, methicillin-resistant, vancomycin-susceptible (MIC ≤ 2mg/L) rifampicin-susceptible *Staphylococcus* or penicillin allergy			
Vancomycin**#** + Rifampicin	As per policy 300mg – 600mg PO/IV 12 hourly	4 weeks 4 weeks	Vancomycin - Pre dose levels 15-20mg/L Always use oral rifampicin if oral route available. Use 300mg bd dose of rifampicin if CrCl< 30mL/min
NVE, methicillin-resistant, vancomycin-resistant (MIC>2mg/L), daptomycin-susceptible (MIC≤1mg/L) *Staphylococcus* spp. or patient unable to tolerate vancomycin			
Daptomycin (Consultant Microbiologist approval required) + Rifampicin **OR** Gentamicin*****	6mg/kg IV 24 hourly 300mg – 600mg PO/IV 12 hourly 1mg/kg IV 12 hourly	4 weeks 4 weeks 4 weeks	Monitor creatine phosphokinase weekly. Adjust dose according to renal function Always use oral rifampicin if oral route available. Use 300mg bd dose of rifampicin if CrCl< 30mL/min
PVE, methicillin, rifampicin- susceptible *Staphylococcus* spp.			
Flucloxacillin + Rifampicin + Gentamicin *	2g IV 6 hourly (<85kg) 2g IV 4 hourly (>85kg) 300mg – 600mg PO/IV 12 hourly 1mg/kg IV 12 hourly	6 weeks 6 weeks 6 weeks	In penicillin allergy use regimen below Always use oral rifampicin if oral route available. Use 300mg bd dose of rifampicin if CrCl< 30mL/min
PVE, methicillin-resistant, vancomycin-susceptible (MIC≤2mg/L), *Staphylococcus* spp. or penicillin allergy			

Vancomycin**#** + Rifampicin + Gentamicin*****	As per policy 300mg – 600mg PO/IV 12 hourly 1mg/kg IV 12 hourly	6 weeks 6 weeks ≥2 weeks	Vancomycin - Pre dose levels 15-20mg/L Always use oral rifampicin if oral route available. Use 300mg bd dose of rifampicin if CrCl< 30mL/min Continue gentamicin for the full course if there are no signs or symptoms of toxicity
PVE, methicillin-resistant, vancomycin-resistant (MIC>2mg/L), daptomycin-susceptible (MIC ≤1mg/L) *Staphylococcus* spp. or patient unable to tolerate vancomycin.			
Daptomycin (Consultant Microbiologist approval required) + Rifampicin + Gentamicin*****	6mg/kg IV 24 hourly 300mg – 600mg PO/IV 12 hourly 1mg/kg IV 12 hourly	6 weeks 6 weeks ≥ 2 weeks	Monitor creatine phosphokinase weekly. Adjust dose according to renal function Always use oral rifampicin if oral route available. Use 300mg bd dose of rifampicin if CrCl< 30mL/min. Continue gentamicin for full course if no signs or symptoms of toxicity

Notes:
Monitoring required. Caution in renal impairment – may need to reduce the dose- see page 13
*****Dose according to ideal body weight – see page 13. Monitoring required –see notes on page 13. Caution in renal impairment. May cause nephrotoxicity.

6.3. Treatment Recommendations for Streptococcal Endocarditis

Table 3: Summary of treatment recommendations for streptococcal endocarditis

Treatment options for streptococci (penicillin MIC ≤0.125mg/L)			
1. Benzypenicillin¤ monotherapy	1.2g IV 4 hourly	4-6∞ weeks	Preferred narrow spectrum regimen, particularly for patients at risk of C.*difficile* or high risk of nephrotoxicity
2. Ceftriaxone monotherapy	2g IV/IM od	4-6∞ weeks	Suitable for Outpatient Parenteral Antibiotic Therapy. Not advised for pts at risk of C. *difficile.*
3. Benzylpenicillin ¤ + Gentamicin	1.2g IV 4 hourly 1mg/kg IV 12 hourly	2 weeks	Not advised for pts with PVE, extra-cardiac foci or infection, any indications for surgery, high risk of nephrotoxicity or at risk of C.*dificile*
4. Ceftriaxone + Gentamicin	2g IV od 1mg/kg IV 12 hourly	2 weeks	Not advised for pts with PVE, extra-cardiac foci or infection, any indications for surgery, high risk of nephrotoxicity or at risk of C.*dificile*
Treatment of streptococci (penicillin MIC > 0.125 to ≤ 0.5mg/L)			
Benzylpenicillin¤ + Gentamicin*	2.4g IV 4 hourly 1mg/kg IV 12 hourly	4 -6 ∞ weeks 2 weeks	Preferred regimen, particularly for patients at risk of C.*difficile*
Treatment of *Abiotrophia* and *Granulicatella* spp. (nutritionally variant streptococci)			
Benzylpenicillin¤ + Gentamicin*	2.4g IV 4 hourly 1mg/kg IV 12 hourly	4-6 ∞weeks 4-6∞ weeks	Preferred regimen, particularly for patients at risk of C.*difficile*
Treatment of streptococci (penicillin MIC > 0.5mgL) **Treatment of streptococci in patients with significant penicillin allergy**			
Vancomcyin# + Gentamicin* **OR** Teicoplanin≈ + Gentamicin*	As per policy 1mg/kg IV 12 hourly 10mg/kg 12 hourly for 2 doses then 10mg/kg od	4-6∞ weeks ≥2 weeks 4-6∞ weeks	Vancomycin - Pre dose levels 15-20mg/L Teicoplanin should be considered for susceptible isolates (NOT staphylococci) when combination with gentamicin required.

	1mg/kg IV 12 hourly	≥2 weeks	Teicoplanin dosing interval adjusted according to renal function as per policy.

Notes:
PVE, prosthetic valve endocarditis; NVE, native valve endocarditis
∞. Use the longer time recommendation for patients with PVE, secondary brain abscesses or vertebral osteomyelitis
¤ Amoxicillin 2g IV every 4-6 hours may be used in place of benzylpenicillin
Monitoring required. Caution in renal impairment – may need to reduce the dose- see page 13.
*****Dose according to ideal body weight – see page 13. Monitoring required –see notes on page 13. Caution in renal impairment. May cause nephrotoxicity
≈ Measure trough levels at least weekly to ensure level of ≥20mg/l and < 60mg/. Levels can not be done on site and need to be sent to Bristol

6.3.1. Treatment Recommendations for Enterococcal Endocarditis

Table 4: Summary of treatment recommendations for enterococcal endocarditis

1. Amoxicillin **OR** Benzylpenicillin + Gentamicin*****	2g IV 4 hourly 2.4g IV 4 hourly 1mg/kg IV 12 hourly	4-6 weeks (6 weeks if PVE) 4-6 weeks (6 weeks if PVE) 4-6 weeks (6 weeks if PVE)	For amoxicillin susceptible (MIC≤ 4mg/L), penicillin susceptible (MIC≤4mg/L) AND gentamicin susceptible (MIC ≤128mg/L) *There should be a low threshold for stopping gentamicin in patients with deterioriating renal function or other signs of toxicity*
2. Vancomycin**#** + Gentamicin*****	As per policy 1mg/kg IV 12 hourly	4-6 weeks (6 weeks for PVE) 4-6 weeks (6 weeks for PVE)	For penicillin-allergic patient or amoxicillin- or penicillin-resistant isolate. Vancomycin - Pre dose levels 15-20mg/L Ensure vancomcyin MIC ≤4mg/L *There should be a low threshold for stopping gentamicin in patients with deterioriating renal function or other signs of toxicity*
3. Teicoplanin**≈** + Gentamicin*****	10mg/kg 12 hourly for 2 doses then 10mg/kg od 1mg/kg IV 12 hourly	4-6 weeks (6 weeks for PVE) 4-6 weeks (6 weeks for PVE)	Consider teicoplanin if significant renal impairment. Teicoplanin dosing interval adjusted according to renal function as per policy. Ensure teicoplanin MIC ≤2mg/L *There should be a low threshold for stopping gentamicin in patients with deterioriating renal function or other signs of toxicity*
4. Amoxicillin	2g IV 4 hourly	≥6 weeks	For amoxicillin-susceptible (MIC≤4mg/L) AND high-level gentamicin resistant (MIC> 128mg/L) isolates Streptomycin 7.5mg/kg IM 12 hourly can be added if isolate susceptible

Notes:

PVE, prosthetic valve endocarditis; NVE, native valve endocarditis

Monitoring required. Caution in renal impairment – may need to reduce the dose- see page 13.

*****Dose according to ideal body weight – see page 13. Monitoring required –see notes on page 13. Caution in renal impairment. May cause nephrotoxicity

≈ Measure trough levels at least weekly to ensure level of ≥20mg/l and < 60mg/. Levels can not be done on site and need to be sent to Bristol

6.4. Treatment Recommendations for Miscillaneous types of Endocarditis

Table 5: Summary of treatment recommendations for Hacek organisms

This organism must be treated in consultation with a medical microbiologist.
The HACEK group of microorganisms are extracellular Gram-negative bacteria which cause an estimated 3% of all cases of IE and include Haemophilus parainfluenzae, Haemophilus influenzae, Haemophilus aphrophilus, Haemophilus paraphrophilus, Actinobacillus actinomycetemcomitans, Cardiobacterium hominis, Eikenella corrodens and kingella spp. Treatment will be directed on the basis of identification and sensitivities.

Amoxicillin sensitive, beta-lactamase negative organisms			
Amoxicillin + Gentamicin*****	2g IV 4-6 hourly 1mg/kg IV 8 hourly	Native valve – 4 weeks Prosthetic valve – 6 weeks 2 weeks only	
Amoxicillin resistant, including beta-lactamase positive organisms; or penicillin allergic patient			
Ceftriaxone + Gentamicin*	2g IV (max 4g) od 1mg/kg IV 8 hourly	Native valve – 4 weeks Prosthetic valve – 6 weeks 2 weeks only	
Oral option			
Ciprofloxacin	500mg PO 12 hourly	Native valve – 4 weeks Prosthetic valve – 6 weeks	

*Dose according to ideal body weight – see page 13. Monitoring required –see notes on page 13. Caution in renal impairment. May cause nephrotoxicity

6.4.1. Treatment Recommendations for Gram-negative Endocarditis

Table 6: Summary of treatment recommendations for Q fever organisms

This organism must be treated in consultation with a medical microbiologist.

Patients should be considered cured when IgG antibodies to C. *burnetii* phase I are < 1:800 and phase I IgM and IgA antibodies are < 1:50.

Doxycycline + Hydroxycholorquine	100mg PO 12 hourly 200mg PO 8 hourly	≥18 months and < 4 years	In slow responders, defined as < 50% reduction in mean phase 1 titres, doxycycline dosing should be adjusted to achieve serum levels of ≤ 5mg/L Plasma levels of hydroxychloroquine to be maintained at 0.8-1.2mg/L. Monthly serum levels must be obtained and dose adjusted accordingly. Photosensitivity is common. Retinal accumulation necessitates regular examination *Antibody titres should be determined every 6 months whilst on treatment and then every 3 months for a minimum of 2 years once treatment has been discontinued.*
OR			
Doxycycline + Ciprofloxacin	100mg PO 12 hourly 500mg PO 8 hourly or 750mg PO 12 hourly	≥ 3 years	In slow responders, defined as < 50% reduction in mean phase 1 titres, doxycycline dosing should be adjusted to achieve serum levels of ≤ 5mg/L *Antibody titres should be determined every 6 months whilst on treatment and then every 3 months for a minimum of 2 years once treatment has been discontinued.*

6.5. Table 7: Summary of treatment recommendations for *Bartonella* endocarditis

This organism must be treated in consultation with a medical microbiologist.

Amoxicillin + Gentamicin*	2g IV 4 hourly 1mg/kg IV 8 hourly	6 weeks 4 weeks	If penicillin allergic use tetracycycline
Penicillin allergy:			
Doxcycline + Gentamicin*	200mg PO 24 hourly 1mg/kg IV 8 hourly	6 weeks 4 weeks	

*Dose according to ideal body weight – see page 13. Monitoring required –see notes on page 13. Caution in renal impairment. May cause nephrotoxicity

Other Gram Negative Bacteria.
Treat in consultation with a medical microbiologist.

A wide range of other Gram-negative bacteria continue to cause a small proportion (<5%) of IE. Risk factors include IV drug use, end-stage liver disease, central venous catheters and old age.

Ever changing resistance patterns, such as the spread of ESBL producing isolates and multidrug resistant strains complicate therapy and preclude clear evidence based recommendations for treatment.

A B-lactam (amoxicillin, cephalosporin or meropenem) and gentamicin (if no concerns about nephrotoxicity) should be used.

Gentamicin: Consider the use of therapeutic (5mg/kg) gentamicin (in patients with good renal function) instead of the low dose synergistic gentamicin used in gram-positive endocarditis.

Prolonged high dose gentamicin carries a significant risk of nephrotoxicity and careful monitoring for toxicity including audiometry is advised for courses longer than 2 weeks.

6.6. Treatment Recommendations for Fungal Endocarditis

This organism must be treated in consultation with a medical microbiologist.

Further information can be obtained from the Trust Guideline for the use of Antifungals in Adults, Trust ID 1263

- Fungal endocarditis comprises 2-4% of all cases. It is most common in IV drug abuse, patients with prosthetic valve endocarditis, neonates and immunocompromised patients.

- The treatment is currently unsatisfactory and usually requires surgical intervention.
- Surgical valve replacement is highly desirable, if technically feasible.
- Treatment should be given for a minimum of 4 weeks but usually much longer and in some circumstances (e.g prosthetic valves) therapy may be life long.
- Susceptibility testing must be undertaken for any fungus causing endocarditis including the determination of minimal fungicidal concentrations.
- If fungi continue to be isolated from blood cultures obtained after 1 week of treatment they should also be susceptibility tested as resistance may emerge on therapy.
- Fungal blood cultures should continue to be taken for at least the first 2 weeks on therapy and if any deterioration occurs, after this.

6.7. Summary Table for Dosage and Monitoring of Antimicrobials

Table 12: Antibiotic Dosing and Monitoring Requirements

Gentamicin	1mg/kg 8-12 hourly (depending on organism. Refer to tables above for specific regime) (IV/IM) i.e. for 70kg patient give 70mg bd or tds depending on organism. **Once daily dosing (5mg/kg)** : Can be considered ONLY for the treatment of gram negative organisms in patients with good renal function (CrCL>60mL/min) after discussion with a consultant medical microbiologist or consultant cardiologist	Pre-dose <1mg/L Post dose 3-5mg/L (although evidence to support this is limited) Take first level pre and post 3rd dose. **Normal renal function:** Monitor gentamicin levels and creatinine twice a week. Patients with infective endocarditis may have variable renal function. **Impaired renal function:** Adjust dose according to creatinine clearance and gentamicin levels. Monitor levels daily until correct levels achieved. Then monitor twice weekly if renal function remains stable. If patients renal function is unstable monitor creatinine and gentamicin levels daily. **Obese Patients:** **Use ideal body weight to calculate the dose. If not obese use actual body weight** Ideal Body Weight ♂ (kg) = 50 + (2.3 x inches over 5 feet) Ideal Body Weight ♀ (kg) = 45.5 + (2.3 x inches over 5 feet)
Vancomycin	Loading and maintenance dose as per specific Vancomycin policy Trust Docs ID: 1192	Pre-dose levels 15-20mg/L. Take first level pre 3rd dose if using once daily regimen or pre 4th dose if using twice daily regimen Adjust dose according to levels.

		Normal renal function: monitor levels twice weekly Impaired renal function: monitor frequency as with gentamicin in impaired renal function See vancomycin policy for further information
Teicoplanin *(only to be used on consultant or consultant microbiologist advice in patients with impaired renal function)*	Loading and maintenance dose as per specific Teicoplanin policy Trust Docs ID: 18469	Pre-dose levels ≥20mg/L (and <60mg/L) Repeat at least weekly Teicoplanin dosing interval adjusted according to renal function as per policy.
B-lactams **Amoxicillin**	IV 2g 4-6 hourly. (depending on organism. Refer to tables above for specific regime)	Dose reduction necessary if CrCl < 10mL/min
Rifampicin	600mg PO BD	Monitor LFTs (Care if in combination with sodium fusidate) Reduce dose if CrCl < 30mL/min to 300mg PO BD Can be given IV if oral route is not available
Sodium fusidate	500mg PO 8 hourly	Monitor LFTS (care if in combination with rifampicin)
Streptomycin (only to be used under the guidance of a medical microbiologist)	7.5mg/kg bd	Pre-dose levels <3mg/L Normal renal function: monitor twice weekly Impaired renal function: Monitor as with gentamicin in impaired renal function
Flucloxacillin	2g IV 6 hourly (<85kg) 2g IV 4 hourly (>85kg)	Dose reduction necessary if CrCL < 10mL/min
Daptomycin (Consultant Microbiologist approval required)	6mg/kg IV 24 hourly (higher doses (unlicensed), usually up to 10mg/kg can be used ONLY on recommendation by a consultant Microbiologist	Monitor creatine phosphokinase weekly. Adjust dose according to renal function Increase the dosing interval to 48 hourly in patients where creatinine clearance is <30ml/min (or post-dialysis).
Hydroxychloroquine	200mg PO 8 hourly	Plasma levels of hydroxychloroquine to be maintained at 0.8-1.2mg/L. Monthly serum levels must be obtained and dose adjusted accordingly. Photosensitivity is common. Retinal accumulation necessitates regular examination
Doxcycyline	200mg PO 24 hourly OR 100mg PO 12 hourly (depending on organism.	In slow responders, defined as < 50% reduction in mean phase 1 titres, doxycycline dosing should be adjusted to achieve serum levels of ≤ 5mg/L

	Refer to tables above for specific regime)	
Ciprofloxacin	500mg PO 8 or 12 hourly or 750mg PO 12 hourly (depending on organism. Refer to tables above for specific regime)	Renal drug database recommends 50-100% of normal dose in CrCl 10-30ml/min Reduce dose to 50% when CrCl < 10ml/min

7. References

Elliot T, Foweraker J, Gould F, Perry J, Sandoe J. 2004. Guidelines for the antibiotic treatment of endocarditis in adults: report of the Working Party of the British Society for Antimicrobial Chemotherapy. Journal of Antimicrobial Chemotherapy.

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Horstkotte D, Follath F, Gutschik E, Lengyel M, Oto A, Pavie A *et al*. 2004. Guidelines on Prevention, Diagnosis and Treatment of infective Endocarditis, Executive Summary. European Heart Journal. 25, 267-276

Wilson W, Karchmer A, .Dajani A, Taubert K, Bayer A, Kaye D *et al*. 1995. Treatment of adults with infective endocarditis due to streptococci, enterococci, staphylococci, and HACEK microorganisms. American Heart Association. Journal of American Medical Association. 274, 21

8. Audit of the policy

Compliance with the process will be monitored through the following:

Key elements	Process for Monitoring	By Whom (Individual / group /committee)	Responsible Governance Committee /dept	Frequency of monitoring
All patients should receive the correct treatment for the correct length of time according to organism and sensitivities.	Audit	Antimicrobial Subcommittee/ Cardiology Consultants	Cardiology/ Microbiology	Biannually
The antibiotics should be monitored according to the guideline	Audit	Antimicrobial Subcommittee/ Cardiology Consultants	Cardiology/ Microbiology	Biannually

The audit results are to be discussed at relevant governance meetings to review the results and recommendations for further action. Then sent to Antimicrobial Subcommittee who will ensure that the actions and recommendations are suitable and sufficient.

9. Equality Impact Assessment (EIA)

Type of function or policy	Existing (remove which does not apply)

Division	Division 4	**Department**	Microbiology
Name of person completing form	Anne Bochmann	**Date**	27/03/2023

Equality Area	Potential Negative Impact	Impact Positive Impact	Which groups are affected	Full Impact Assessment Required YES/NO
Race	None	None	N/A	No
Pregnancy & Maternity	Contraindication of certain medications in pregnancy and breastfeeding	None	N/A	No
Disability	None	None	N/A	No
Religion and beliefs	None	None	N/A	No
Sex	None	None	N/A	No
Gender reassignment	None	None	N/A	No
Sexual Orientation	None	None	N/A	No
Age	None	None	N/A	No
Marriage & Civil Partnership	None	None	N/A	No
EDS2 – How does this change impact the Equality and Diversity Strategic plan (contact HR or see EDS2 plan)?				

- **A full assessment will only be required if: The impact is potentially discriminatory under the general equality duty**
- **Any groups of patients/staff/visitors or communities could be potentially disadvantaged by the policy or function/service**
- **The policy or function/service is assessed to be of high significance**

IF IN DOUBT A FULL IMPACT ASSESSMENT FORM IS REQUIRED

The review of the existing policy re-affirms the rights of all groups and clarifies the individual, managerial and organisational responsibilities in line with statutory and best practice guidance.